IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS	:	Breitenbach et al.
SERIAL NO.	:	12/141,489
FILING DATE	:	June 18, 2008
FOR	:	HIGHLY PURITY BASES OF 3,3-DIPHENYLPROPYLAMINO MONOESTERS
EXAMINER	:	Valeurod
GROUP ART UNIT:		1621

COMMISSIONER FOR PATENTS
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DECLARATION OF RALF KANZLER UNDER 37 C.F.R. § 1.132

I, Ralf Kanzler, declare the following:

1. I am a German citizen residing at Dürerstrasse 23, 51371 Leverkusen, Germany.

2. I am currently an employee of UCB Pharma GmbH, formerly Schwarz Pharma AG, the assignee of U.S. Patent Application Serial No. 12/141,489. A copy of my curriculum vitae is attached.

3. Prior to April 8, 2003, the priority date of U.S. Patent Application Serial No. 141,489, I attempted to purify fesoterodine free base by chromatography and by re-crystallization. Both attempts failed. Furthermore, an attempt to purify fesoterodine free base by distillation was made by another person working under my supervision. That attempt also failed.

Chromatographic approaches

4. Separation via silica gel chromatography: Separation through silica gel using medium and apolar solvents and various tert-amine compound additions was carried out. The separations were first assessed through thin layer chromatography. The following eluent mixture turned out to work best: 20 Vol% Acetone/ 70 Vol% Petrolether/ 10 Vol% Triethylamine.

5. The application of the above eluent mixture, however, to column chromatography (both MPLC & HPLC) failed. The product was totally absorbed by the silica gel.

6. From the above, I concluded that silica gel chromatography:

- resulted in a high loss of the compound;
- gave very poor separation; and
- required tremendous amounts of eluent.

7. Separation through RP 18 Phases: The separation was first assessed through thin layer chromatography using the following.

- aqueous/aprotic organic mixtures with and without base additions; and
- aqueous/protic organic mixtures with and without base additions.

8. Depending on the water content, either adsorption or displacement of the base was observed at the mobile phase borderline. In other words, a low water content causes fesoterodine to flow (eluate) poorly, while a high water content causes fesoterodine to flow at the borderline of the aqueous phase (the product is transported without interaction with the stationary phase). In either case, purification of the free base did not occur.

9. Chromatographic separations using acid eluents were not possible as they would have transformed fesoterodine into its acid addition salt.

Re-crystallization approaches

10. All of the usual more or less polar solvents were used in attempts to obtain purified fesoterodine free base through re-crystallization, but all attempts failed.

Distillation approach

11. Exhibit A is a copy of a lab-journal report that describes a failed attempt to purify fesoterodine free base by distillation. Exhibit A is in German; Exhibit B is an English translation of Exhibit A.

12. The work shown in Exhibits A and B was carried out by Ms. T. Schröder, working under my supervision.

13. Exhibits A and B describe an attempt to purify fesoterodine base by distilling fesoterodine base, which was in the form of an oil. The attempt did not succeed, as the oil could not be distilled.

14. To summarize: three different general purification approaches were tried, namely distillation, chromatography and direct crystallization. All attempts failed to produce fesoterodine free base.

Statements herein based on my own knowledge are true. I acknowledge that willful false statements are punishable by fine or imprisonment as provided for by 18 U.S.C. § 1001 and may jeopardize the validity or enforceability of any patent that may mature from the present Application.

Signed 24. Aug, 2010

Ralf Kanzler

CV - Ralf Kanzler

Birth Date / Place	01. July 1953 / Leverkusen (Germany)
Nationality	German
School education	Secondary School
Professional Education	31. August 1969 to 31.August.1972 : Education leading to the degree of a laboratory assistant at Bayer AG in Leverkusen (Germany) 01.October 1974 to 16.July 1976 : Study of Chemistry at the Rhineland Academy in Cologne; awarded by the degree of a Chemical Assistant
Job Experience	
01. September 1972 to 30. September 1974	Chemical Assistant at Bayer AG in Leverkusen / Germany Focus on : • Process improvements for the manufacture of intermediate products of the dye, polymer and pharmaceutical industry; • Purification of out-of-specification products in industrial scale
02. November 1976 to 31. January 1977	Chemical Assistant at Götze AG in Burscheid / Germany
01. April 1977 - today	Schwarz Pharma AG, now UCB Pharma GmbH Focus on : • Synthesis of metabolites • Isolation of substances from complex compound mixtures through chromatographic methods (HPLC, MPLC)

	• Development of synthetic procedures for technical up-scale • Planning and performance of up-scale processes in kilo-laboratory with non –GMP as well as GMP status • Responsible for GMP standard in the kilo laboratory • Setting up of synthetic procedures for GMP-manufacture • Documentation of synthesis (reports, lab-journals)
Special expertise	Handling of radioactive materials